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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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11/15/2001

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EXAMINER

MCKENZIE, THOMAS C

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 11/15/2001

*JS*

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/450,999

Applicant(s)

PORTER ET AL.

Examiner

Thomas McKenzie Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 09 October 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 2-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

1. This action is in response to amendments filed on 10/9/01. Applicants have amended claims 16-18. There are twenty-one pending claims. Claims 2-14 and 16 are compound claims. Claim 15 is a composition claim. Claims 17-22 are use claims. This is the fourth action on the merits. Claims 2-22 were previously rejected. The application concerns  $\beta$ -amidobenzenepropanoic acid compounds.

***Response to Amendment***

2. Applicants' deletion of "prophylaxis" from claim 17 overcomes the enablement rejection made in point #3 of the office action of 5/30/01. Applicants' deletion of "multiple sclerosis" from claim 18 overcomes the enablement rejection made in Point #4 of that office action. Applicants' deletion of the three provisos from claim 16 overcomes the new matter rejection made in point #5. Deletion of  $R^3 = \text{alkyl}$  and  $L^1 = \text{ester}$  overcomes the art cited in paper #14, the second action on the merits. Thus, these provisos are no longer needed. Applicants' amendment to claim 16 specifying that they intend by ester and amide overcomes the indefiniteness rejection made in point #9. The Examiner is reading these terms to be  $\text{CO}_2\text{R}$  and  $\text{CONH}_2$  respectively where R is an alkyl group. Applicants' deletion of the limitation in claim 16 that  $R^3$ , the group attached to  $R^1$  can be aliphatic overcomes the anticipation rejections over Kato (Tetrahedron Lett.) and Alig ('282) made in points #11 and #13. The two references teach only alkyl groups at

R<sup>3</sup>. The R<sup>3</sup> group in Scott ('773) is a substituted alkyl group, thus no longer falling within Applicants' claim.

***Claim Rejections - 35 USC § 112***

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 2-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the last line of both claim 14 and claim 16, Applicants have the word "solvates". This reads on an unlimited and undefined number of solvent complexes with Applicants' claimed compounds. What solvents are envisioned? The Examiner suggests deleting the term.

Applicants argue that breadth is not to be confused with indefiniteness. This is not persuasive. The Examiner in the previous action asked some specific questions regarding the claimed solvents and solvates. If the Applicants cannot answer the question, then how is the public to understand the meets and bounds of the limitation? Not all solvents form solvates with a particular crystalline molecule. The stoichiometry of solvate formation can range from one solvent per four or eight host molecules to three solvents per host molecule and is not predictable in advance. Nowhere in the specification are descriptions of preparing any solvates to be found.

4. Claims 2-13 and 15-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants repeatedly claim "optionally substituted" in reference to their aliphatic, heterocycloaliphatic etc groups. This is indefinite because we do not know what these substituents are or where there are to be placed. The Examiner suggests that these substituent groups be spelled out in the claims so that we know what Applicants intend. For example, in the lines spanning pages 3 and 4 of the amendments Applicants do definitely claim what they intend for R<sup>b</sup>. In lines 8-22 of page 7, Applications use open language to indicate possible aromatic or heteroaromatic substituents. In the passage spanning line 14, page 13 to line 4, page 14 there is a second, conflicting, open language indication of possible aromatic or heteroaromatic substituents. Possible aliphatic substituents are suggested in lines 27-34 of page 10. In each case, since open language is used, what other substituents are being claimed.

Applicants request clarification regarding the open language and the conflicting definitions of "optionally substituted". It is provided above. Applicants also state that they do not intend the dictionary definition of substituent but rather prefer their own. While applicant may be his or her own lexicographer,

a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947).

5. Claims 2-13 and 15-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 16, Applicants repeatedly refer to “heteroaliphatic”, “cycloaliphatic”, and “polycycloaliphatic” and “hetero polycycloaliphatic”. These are all improper. To quote from Hawley (The Condensed Chemical Dictionary) “aliphatic ... characterized by straight- or branched-chain arrangement of the constituent carbon atoms.” An aliphatic group may be saturated or unsaturated. An aliphatic group may not contain rings or hetero atoms. Applicants’ terms “heteroaliphatic”, “cycloaliphatic”, and “polycycloaliphatic” and “hetero polycycloaliphatic” are not recognized in the art of organic chemistry and are oxymorons. Thus, we do not know what Applicants intend by these unique terms since the prefixes conflict with the stem word aliphatic. The Examiner suggests “alicyclic” and “heterocyclic” if that is what they intend.

There are three problems with Applicants’ terms. Firstly, “aliphatic” itself has been held to be too broad, reading on double, triple, conjugated double bonds, interfering reactive groups, as well as non-carbon linkages. From footnote 3 *In re*

*CAVALLITO AND GRAY*, 134 USPQ 370, decided by the U.S. Court of Customs and Patent Appeals we learn there are conflicting definitions of the term, "aliphatic--Organic compounds whose molecules do not have their carbon atoms arranged in a ring structure. This category therefore includes all the paraffin hydrocarbons and their saturated and unsaturated derivatives of all types. [Emphasis added.] (The Condensed Chemical Dictionary, 6th Ed., p. 38). aliphatic compounds--Aliphatic compounds are organic compounds having an open-chain (noncyclic or acyclic) carbon skeleton. The term "aliphatic" is derived from aleiphatos, the Greek word for fat, which is the source of many of the aliphatic compounds. Aliphatic compounds include paraffin hydrocarbons, olefins (ethylenic hydrocarbons), and acetylenic hydrocarbons, and their derivatives of all types. [Emphasis added.] (Encyclopedia of Chemical Technology, Vol. 1, Kirk and Othmer, p. 356). aliphatic \* \* \*: Fatty, acyclic--used of a large class of organic compounds characterized by an open-chain structure and consisting of the paraffin, olefin and acetylene hydrocarbons and their derivatives (as the fatty acids); distinguished from alicyclic, aromatic, heterocyclic [Žterpenes] [emphasis added.] (Webster's Third New International Dictionary, p. 53)." The court concluded that "[t]here is no question but the term in question in rejected claims 1 and 35 is such a broad term that it will embrace subject matter not

disclosed in the specification. The specification does not disclose any factors governing the selection of the claimed "three lower-aliphatic groups,"

Secondly, the definition given by Webster's specifically excluded alicyclic compounds, thus what is one to make of "cycloaliphatic"? Thirdly, the term "heteroaliphatic" could mean several things. Is it an aliphatic substituted by a heterocycle, e.g. pyridyl-methyl? An aliphatic interrupted by a heteroatom, such as methoxymethyl? An aliphatic substituted by a heteroatom, e.g. chloromethyl? Whatever choice is selected must be supported by the specification.

6. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a disease or disorder in a mammal in which the extravascation of leukocytes plays a role" is indefinite for reasons stated previously.

Applicants have argued that the passage on page 22, lines 8-11 exemplifies what diseases they intend. This is not persuasive for three reasons. Firstly, the word "includes" in this passage is open language. What additional specific diseases do Applicants intend to treat? Secondly, search of the "Merck Manual of Diagnosis and Therapy, 16th Edition", and the medical school textbook "Cecil Textbook of Medicine, 20th Edition" reveals no entries for "extravascation of



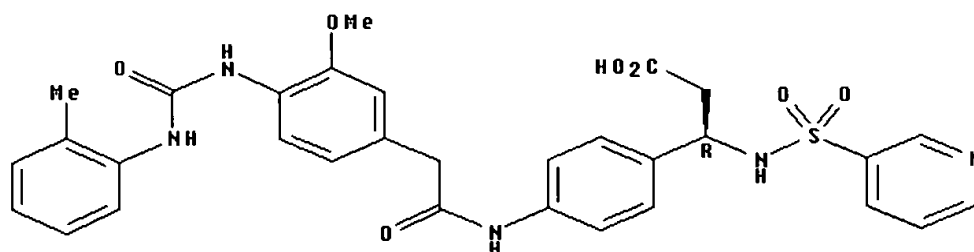
leukocytes””. Thus, one of ordinary skill in the clinical arts would have no clue as to the meaning of “a disease or disorder in a mammal in which the extravascation of leukocytes plays a role”. Thirdly, how specific of a role must the leukocytes play in a disease for it to be covered by the claim? Must it be the sole mechanism of the disease process or will any role suffice?

The Examiner suggests selecting some of the specifically listed diseases from lines 9-11, page 22. Claimed treatment of multiple sclerosis would raise enablement questions unless Applicants can point to any  $\alpha_4\beta_1$  integrin binding inhibitor, which has demonstrated clinical efficacy, or unless Applicants can show an art recognized correlation between their assays and such clinical efficacy against MS

***Claim Rejections - 35 USC § 102***

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 2-10, 12, 13, and 15-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Astles (WO 99/23063 A1). There are thirty-one compounds in this reference which anticipate Applicants' claims. The one shown below has  $Ar^1$  = phenyl substituted by [3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino] phenyl,  $r = 1$ ,  $L^1 = -CONH-$ ,  $Ar^2 = 1,4$ -phenylene,  $R^1 = SO_2C_5H_4N$ ,  $R^3 = \text{pyridyl}$ ,  $R^a = R^{a'} = \text{hydrogen}$ , and  $R = CO_2H$ . It is found in Example 3, page 70 lines 11-14. See also claims 26-34 39, and 45

concerning claimed Y and R<sup>15</sup> groups. A copy of the Chemical Abstracts search on this reference is provided for Applicants' convenience. Should this reference issue as a US patent, it would be a 102(e) reference against Applicants' claims.



### *Interference*

8. Applicants' attention is drawn to Schoop ('503). Applicants have support in their British application 9826174.6 for their claims. Thus, Schoop ('503) is not a competent 102(e) reference against Applicants' claims. However there is overlapping claimed subject matter. The variable L, R4, and R4' in claims 1-8 and 12-14 of Schoop ('503) correspond to Applicants' variables L1, R1, and R3 respectively and provoke an interference with Applicants' claims 2-10, 12, 13, and 15-17.

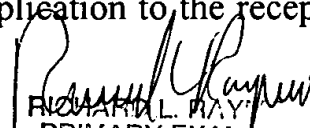
### *Allowable Subject Matter*

9. Claims 9, 13, and 14 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

***Conclusion***

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for the Examiner is (703) 746-3152. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mukund Shah can be reached on (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

  
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PRIMARY EXAMINER  
ART UNIT 1624

**Mukund Shah**  
**Supervisory Patent Examiner**  
**Art Unit 1624**

TCMcK  
November 9, 2001

